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PATENT  
Attorney Docket No.: 020048-004200US

TOWNSEND and TOWNSEND and CREW LLP

By: Patricia Ambers

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Byung Sook Moon  
Martin Jones  
Johnny Valdez

Application No.: 10/672,266

Filed: September 25, 2003

For: LYOPHILIZED BEADS  
CONTAINING MANNITOL

Confirmation No. 8805

Examiner: Pande, Suchira

Technology Center/Art Unit: 1637

**APPELLANTS' REPLY BRIEF UNDER  
37 CFR §41.41**

Mail Stop Appeal Brief  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Commissioner:

Further to the Examiner's Answer mailed September 17, 2009, Appellant submits this  
Reply Brief under 37 CFR §41.41. A **Request for Oral Hearing** is filed concurrently herewith.

**Remarks** begins on page 2 of the Reply Brief.

**Proposed Claim Amendments** are reflected in the amended claim 1 on page 5 of the  
Reply Brief.

### REMARKS

The Examiner has maintained the pending rejections to the claims for failing to comply with the written description requirement under 35 U.S.C. § 112, 1st paragraph, and obviousness under 35 U.S.C. § 103(a) over Park and Trem1, alone and in combination with Kellogg or Shively. Applicant responds to the Examiner's Answer below.

Applicant also proposes amending claim 1 to remove from the claims the terms "about" in regards to the claimed range, and the term "substantially" in regards to the spherical nature of the claimed beads. Applicant believes such amendments would render moot the pending rejections. Although Applicant recognizes that claim amendments cannot be entered at this point of appeal as of matter of right, the proposed claim 1 is provided for consideration by the Examiner and the Board.

The Examiner has raised two new arguments in the Examiner's Response that are addressed in turn below.

#### **I. THE EXAMINER HAS IMPROPERLY EXPANDED APPLICANT'S CLAIMED RANGE BY APPLYING A NONSENSICAL VARIANCE THEORY**

In modifying the rejection of the claims under 35 U.S.C. §103, the Examiner now asserts that the lower limit of the range recited in claim 1 for mannitol should be interpreted to be 42% rather than the claimed 53%:

The range claimed by Applicant is between about 53% and about 75%. Since upper limit is about 75% and lower limit is about 53%, hence this claimed range includes a variance of  $(75-53/2 = 22/2 = 11)$  +/- 11%. So the lower limit of the claimed range is  $53 - 11 = 42\%$ .

This conclusion is contrary to the consensus reached by the Examiner and Applicant's representative during a telephonic interview of June 4, 2007 which the Examiner summarized as follows:

During interview of June 4, 2007 consensus was reached that Trem1 does not disclose compositions in the range between [about] 53% and about 75%. The range disclosed by Trem1 would be about 45% (w/w).

(See Final Office Action of April 8, 2008.) Based on the new variance theory set forth by the Examiner, however, the Examiner now concludes that the teaching of 45% polyol in Trem1 "falls within the lower limit of the range claimed by Applicant." (Examiner's Answer on page 7, first paragraph.) This conclusion is wrong for at least the following three reasons.

First, the Examiner's theory ignores the plain meaning of the claim. Each range recited in the claims is defined by a specific upper and lower bound. This is fully within Applicant's right under 35 U.S.C. §112, second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention. (Emphasis added.)

To re-interpret a range of "between 53% and 75%" to mean "between 42% and 86%", as the Examiner has now done, completely contravenes the clear meaning of the affected claims. Nor does such a reinterpretation have any basis in the Applicant's specification.

Second, the Examiner's use of variance is mathematically erroneous. Variance is the expected square deviation of a *random variable or distribution* from its expected value or mean.<sup>1</sup> The upper and lower limits, however, do not constitute a distribution at all – they define a range.

Third, rather than calculating a variance as the Examiner alleges, the Examiner has merely calculated how far the upper and lower limits of the range are from their average:  $75-53/2=22/2=11$ . Applicant fails to understand how such a calculation is meaningful or relevant to the present claims.

In summary, the claimed ranges mean what they say, and they cannot be arbitrarily expanded by imposing a variance theory as proposed by the Examiner. Moreover, dependent claims 5 and 6 are separately patentable because by reciting narrower ranges of mannitol than parent claim 1, they are further distinguished over the cited art.

## **II. BEADS CONTAINING 72% TREHALOSE ARE NOT SUBSTANTIALLY SPHERICAL**

The Examiner also newly asserts that the beads having 72% trehalose (w/w) (Part A of Figure 1) are substantially spherical (page 13 of Examiner's Answer). Based on this conclusion, the Examiner alleges that "beads made with sugars other than mannitol and having w/w percentages that are within the claimed range of mannitol are also 'substantially spherical in shape'." Applicant respectfully disagrees because the pictures of beads provided in Figure 1 of the application show that beads other than those having between about 53% and about 75% (w/w) of mannitol are *not* substantially spherical.

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<sup>1</sup> *An Introduction to Mathematical Statistics and Its Applications*, 1981, Prentice-Hall, Inc., Englewood Cliffs, NJ, pp. 113-118.

Figure 1 of the instant application provides a direct comparison of beads prepared using 72% (w/w) trehalose and the claimed mannitol beads (see parts A and E). As stated in the declaration by Martin Jones filed with the Amendment of July 12, 2007 ("the Jones declaration", see also Evidence Appendix 1 and 2 of the Appeal Brief), the trehalose beads "form a shiny, clear, irregular shaped mass that adheres to the bottom of the container, even where the % (w/v) of trehalose matches that of mannitol" (paragraph 6 of the Jones declaration). Thus, Jones, a person of ordinary skill in the art, finds that the trehalose beads are *not* substantially spherical.

In contrast to the *unspherical trehalose* beads, the mannitol beads of the present invention are "smooth and spherical" at 60% and 65% (w/w), within the claimed range. The Jones declaration concludes that "it is ... surprising that exchanging mannitol for trehalose at similar % w/v, affords reproducibly spherical beads having a smooth morphology" (paragraph 6 of the Jones declaration). Thus, Applicant submits that beads made with sugars other than mannitol within the claimed range, are *not* substantially spherical.

### CONCLUSION

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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**PROPOSED CLAIM AMENDMENT**

1. (Proposed Amendment) A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, said lyophilized bead being ~~substantially~~ spherical in shape and comprising:

a thermally stable enzyme; and  
mannitol;

wherein said lyophilized bead has a weight percentage of said mannitol of between ~~about~~ 53% and ~~about~~ 75% (w/w).